## This Page Is Inserted by IFW Operations and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

## IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

In response to the Advisory Action of February 18, 2004 in the above-identified application, please amend the application as follows:

## IN THE SPECIFICATION

At page 1, please replace the original structural formula with the following:

Page 1, lines 18-19, please insert the following:

 $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ , same or different, are a group chosen among: -CONR-, -NRCO--CH<sub>2</sub>-NR-, -NR-CH<sub>2</sub>- where R is H,  $C_{1-3}$  alkyl, <u>or</u> benzyl;

5

10

25

Page 1, lines 22-27, please insert the following:

-(CH<sub>2</sub>)<sub>r</sub> Ar<sub>4</sub> where r is 0, 1 or 2 and Ar is an aromatic group chosen among benzene, naphthalene, thiopene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, possibly substituted with up to 2 substituents chosen among C<sub>1-3</sub> alkyl, C<sub>1-3</sub> haloalkyl, C<sub>1-3</sub> alkyloxy and C<sub>2-4</sub> amino-alkyloxy, halogens, OH, NH<sub>2</sub>, CN, NR<sub>6</sub>R<sub>7</sub>, where R<sub>6</sub> and R<sub>7</sub>, are the same or different, and are H or C<sub>1-3</sub> alkyl,

At page 2, lines 2-12, please replace with the following:

--R<sub>9</sub> is a methanesulfonyl, tosyl, tetrahydropyranyl, tetrahydrothiopyranyl possible mono or disubstituted by oxygen on the S atom, piperidyl possibly optionally substituted on the N atom by a C<sub>1-3</sub> alkyl, C<sub>1-3</sub> acyl, aminosulfonyl or methanesulfonyl; or a group (CH<sub>2</sub>)<sub>g</sub>R<sub>10</sub> where g g is 1,2, or 3 and R<sub>10</sub> is chosen among morpholine, furan, or CN; or R<sub>8</sub> and R<sub>9</sub> together with the N atom to which they are linked form a piperazine possibly optionally substituted at the other N atom one of its nitrogen atoms by C<sub>1-3</sub> alkyl, C<sub>1-3</sub> acyl or methanesulfonyl:--

At page 2, lines 13-21, please insert the following:

- -N(R<sub>11</sub>)CO(CH<sub>2</sub>)<sub>h</sub>-R<sub>12</sub> where R<sub>11</sub> is H/or C<sub>1-3</sub> alkyl; h is 0, 1, 2 or 3; and R<sub>12</sub> is chosen among: morpholine, pyrrolidine possibly substituted with an hydroxy or an hydroxymethyl, piperidine possibly substituted with a group hydroxy, carboxyamido or aminosulfonyl, piperazine possibly substituted on the N-atom by C<sub>1-3</sub> alkyl, triazole, tetrazole, 5-mercapto-tetrazole, furan, thiophene, thiomorpholine possibly mono or di-oxygenated on the S-atom, and amino-cyclohexane possibly substituted by an hydroxy group/; or
- -COR $_{13}$  wherein  $R_{13}$  is morpholine or piperazine possibly substituted with a  $C_{2\text{-}6}$
- alkyl containing one or more ether or hydroxy groups ; and Rs is H.

At page 4, line 3, please insert:

--R<sub>1</sub> and R<sub>2</sub> same or different, are: --

At page 4, lines 14-27, please replace with the following:

- R9<sub>2</sub> is chosen among: methanesulfonyl, tosyl, tetrahydropyranyl, tetrahydrothiopyranyl possibly mono or di-substituted by oxygen on the S atom, piperidyl possibly substituted on the N-atom by a C1-3<sub>1-3</sub> alkyl, C1-3<sub>1-3</sub> acyl, aminosulfonyl or methanesulfonyl; or a group (CH2<sub>2</sub>) g-R<sub>10</sub> where g is 1, 2 or 3 and R<sub>10</sub> is chosen among morpholine, furan or CN;
- or R<sub>8</sub> and R<sub>9</sub> together with the N atom to which they are linked form a piperazine possibly substituted on the other N atom with a C1-3<sub>1-3</sub> alkyl, C1-3<sub>1-3</sub> acyl or methanesulfonyl;
  - -N(R<sub>11</sub>)CO(CH<sub>2</sub>)<sub>h</sub>-R<sub>12</sub> where R<sub>11</sub> is H or C<sub>1-3</sub> alkyl; h is 0, 1, 2, or 3;
  - and R<sub>12</sub> is chosen among: morpholine, pyrrolidine possibly optionally substituted with an hydroxy or hydroxymethyl, piperidine possibly optionally substituted with a group 4-hydroxy, or 4-carboxyamido group or aminosulfonyl, piperazine possibly optionally substituted on the other N-
- atom by C<sub>1-3</sub> alkyl, triazole, tetrazole, 5-mercapto-tetrazole, furan, thiophene thiomorpholine possibly optionally mono or di-oxygenated on the S-atom amino-cyclohexane possibly substituted by an hydroxy group :--

At page 5, lines 11-14, please replace with the the following:

--An even more preferred group of compounds according to the invention are those wherein R, R1<sub>1</sub>, R2<sub>2</sub>, R3<sub>3</sub>, f, m are as above defined and:

R44is a group NR88R99 wherein:

R\$8 is H or methyl;